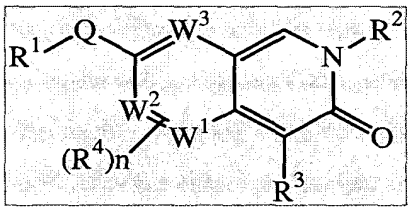
# CLAIMS

What is claimed is:

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

$R^1$ is independently selected from:

$C_5$ or $C_6$ cycloalkyl-($C_1$-$C_8$ alkylenyl);

Substituted $C_5$ or $C_6$ cycloalkyl-($C_1$-$C_8$ alkylenyl);

$C_8$-$C_{10}$ bicycloalkyl-($C_1$-$C_8$ alkylenyl);

Substituted $C_8$-$C_{10}$ bicycloalkyl-($C_1$-$C_8$ alkylenyl);

5- or 6-membered heterocycloalkyl-($C_1$-$C_8$ alkylenyl);

Substituted 5- or 6-membered heterocycloalkyl-($C_1$-$C_8$ alkylenyl);

8- to 10-membered heterobicycloalkyl-($C_1$-$C_8$ alkylenyl);

Substituted 8- to 10-membered heterobicycloalkyl-($C_1$-$C_8$ alkylenyl);

Phenyl-($C_1$-$C_8$ alkylenyl);

Substituted phenyl-($C_1$-$C_8$ alkylenyl);

Naphthyl-($C_1$-$C_8$ alkylenyl);

Substituted naphthyl-($C_1$-$C_8$ alkylenyl);

5- or 6-membered heteroaryl-($C_1$-$C_8$ alkylenyl);

Substituted 5- or 6-membered heteroaryl-($C_1$-$C_8$ alkylenyl);

8- to 10-membered heterobiaryl-($C_1$-$C_8$ alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-($C_1$-$C_8$ alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5- or 6-membered heteroaryl;

Substituted 5- or 6-membered heteroaryl;

8- to 10-membered heterobiaryl;

Substituted 8- to 10-membered heterobiaryl;

$R^2$ is independently selected from:

H;

$C_1$-$C_6$ alkyl;

Phenyl-($C_1$-$C_8$ alkylenyl);

Substituted phenyl-($C_1$-$C_8$ alkylenyl);

Naphthyl-($C_1$-$C_8$ alkylenyl);

Substituted naphthyl-($C_1$-$C_8$ alkylenyl);

5- or 6-membered heteroaryl-($C_1$-$C_8$ alkylenyl);

Substituted 5- or 6-membered heteroaryl-($C_1$-$C_8$ alkylenyl);

8- to 10-membered heterobiaryl-($C_1$-$C_8$ alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-($C_1$-$C_8$ alkylenyl);

Phenyl-O-($C_1$-$C_8$ alkylenyl);

Substituted phenyl-O-($C_1$-$C_8$ alkylenyl);

Phenyl-S-($C_1$-$C_8$ alkylenyl);

Substituted phenyl-S-($C_1$-$C_8$ alkylenyl);

Phenyl-S(O)-($C_1$-$C_8$ alkylenyl);

Substituted phenyl-S(O)-($C_1$-$C_8$ alkylenyl);

Phenyl-$S(O)_2$-($C_1$-$C_8$ alkylenyl);

Substituted phenyl-$S(O)_2$-($C_1$-$C_8$ alkylenyl);

Each substituted $R^1$ and $R^2$ group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

$C_1$-$C_6$ alkyl;

CN;

$CF_3$;

HO;

($C_1$-$C_6$ alkyl)-O;

($C_1$-$C_6$ alkyl)-$S(O)_2$;

$H_2N$;

($C_1$-$C_6$ alkyl)-N(H);

$(C_1\text{-}C_6$ alkyl$)_2$-N;

$(C_1\text{-}C_6$ alkyl$)$-C(O)O-$(C_1\text{-}C_8$ alkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)$-C(O)O-(1- to 8-membered heteroalkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)$-C(O)N(H)-$(C_1\text{-}C_8$ alkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)$-C(O)N(H)-(1- to 8-membered heteroalkylenyl$)_m$;

$H_2NS(O)_2$-$(C_1\text{-}C_8$ alkylenyl$)$;

$(C_1\text{-}C_6$ alkyl$)$-N(H)$S(O)_2$-$(C_1\text{-}C_8$ alkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)_2$-$NS(O)_2$-$(C_1\text{-}C_8$ alkylenyl$)_m$;

3- to 6-membered heterocycloalkyl-$(G)_m$;

Substituted 3- to 6-membered heterocycloalkyl-$(G)_m$;

5- or 6-membered heteroaryl-$(G)_m$; and

Substituted 5- or 6-membered heteroaryl-$(G)_m$;

$(C_1\text{-}C_6$ alkyl$)$-$S(O)_2$-N(H)-C(O)-$(C_1\text{-}C_8$ alkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)$-C(O)-N(H)-$S(O)_2$-$(C_1\text{-}C_8$ alkylenyl$)_m$;

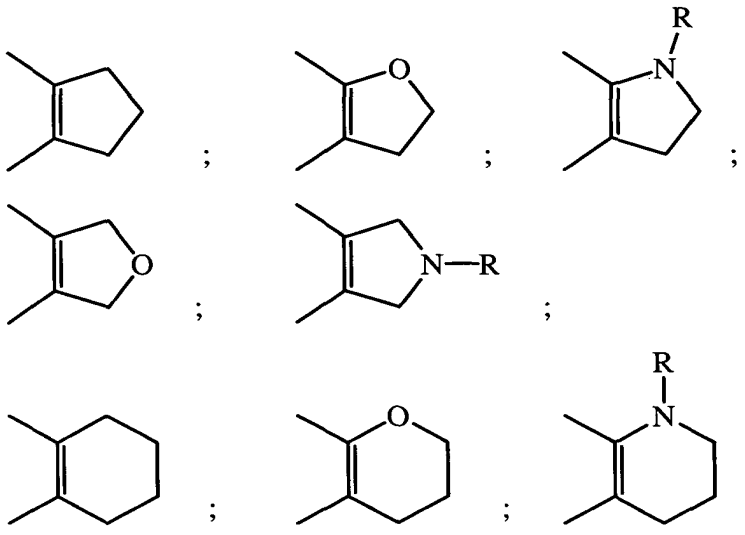
wherein each substituent on a carbon atom may further be independently selected from:

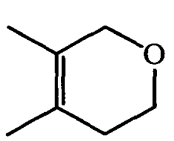
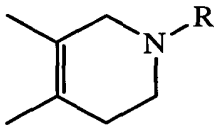
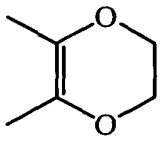
Halo; and

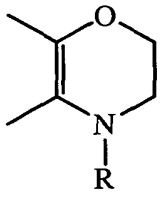
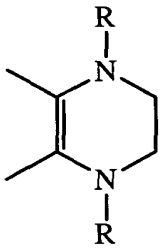
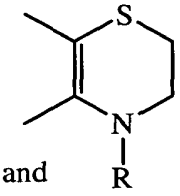
$HO_2C$;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially $sp^2$ carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:




;

;

;


;

; and

;

R is H or $C_1$-$C_6$ alkyl;

G is $CH_2$; O, S, S(O); or $S(O)_2$;

Each m is an integer of 0 or 1;

$R^3$ is selected from the groups:

H;

$C_1$-$C_6$ alkyl;

Substituted $C_1$-$C_6$ alkyl;

$C_2$-$C_6$ alkenyl;

Substituted $C_2$-$C_6$ alkenyl;

$C_2$-$C_6$ alkynyl;

Substituted $C_2$-$C_6$ alkynyl;

$C_3$-$C_6$ cycloalkyl;

Substituted $C_3$-$C_6$ cycloalkyl;

$C_3$-$C_6$ cycloalkyl-($C_1$-$C_8$ alkylenyl);

Substituted $C_3$-$C_6$ cycloalkyl-($C_1$-$C_8$ alkylenyl);

Phenyl;

Substituted phenyl;

Phenyl-($C_1$-$C_8$ alkylenyl);

Substituted phenyl-($C_1$-$C_8$ alkylenyl);

Naphthyl;

Substituted Naphthyl;

Naphthyl-($C_1$-$C_8$ alkylenyl);

Substituted naphthyl-($C_1$-$C_8$ alkylenyl);

3- to 6-membered heterocycloalkyl;

Substituted 3- to 6-membered heterocycloalkyl;

3- to 6-membered heterocycloalkyl-($C_1$-$C_8$ alkylenyl);

Substituted 3- to 6-membered heterocycloalkyl-($C_1$-$C_8$ alkylenyl)

HO;

($C_1$-$C_6$ alkyl)-O;

$H_2N$;

($C_1$-$C_6$ alkyl)-N(H);

($C_1$-$C_6$ alkyl)$_2$-N;

Each substituted $R^3$ group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

$H_2N$;

$C_1$-$C_6$ alkyl;

CN;

$CF_3$;

($C_1$-$C_6$ alkyl)-OC(O);

HO;

($C_1$-$C_6$ alkyl)-O;

HS; and

($C_1$-$C_6$ alkyl)-S;

wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

$HO_2C$;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

$R^4$ is H, $C_1$-$C_6$ alkyl, $H_2N$, HO, or halo;

n is an integer of from 0 to 3;

Q is selected from:

OC(O);

$CH(R^5)C(O)$;

$OC(NR^5)$;

$CH(R^5)C(NR^5)$;

$N(R^5)C(O)$;

$N(R^5)C(S)$;

$N(R^5)C(NR^5)$;

$N(R^5)CH_2$;

$SC(O)$;

$CH(R^5)C(S)$;

$SC(NR^5)$;

trans-(H)C=C(H);

cis-(H)C=C(H);

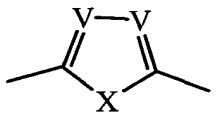
C≡C;

$CH_2C{\equiv}C$;

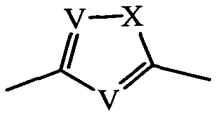
$C{\equiv}CCH_2$;

$CF_2C{\equiv}C$; and

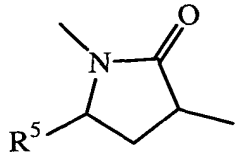
$C{\equiv}CCF_2$;



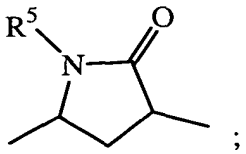
;



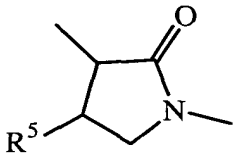
;



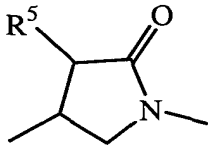
;



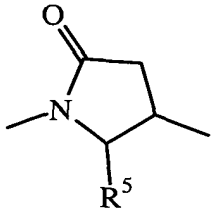
;



;



; and



;

$R^5$ is H, $C_1$-$C_6$ alkyl, $C_3$-$C_6$ cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

X is O, S, N(H), or N($C_1$-$C_6$ alkyl);

Each V is independently C(H) or N;

Each $W^1$, $W^2$, and $W^3$ is independently N or C-$R^4$, wherein $R^4$ is as defined above;

wherein each $C_8$-$C_{10}$ bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 $N(C_1\text{-}C_6$ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 $N(C_1\text{-}C_6$ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 $N(C_1\text{-}C_6$ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and $N(C_1\text{-}C_6$ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 $N(C_1\text{-}C_6$ alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any $(C_1\text{-}C_6$ alkyl$)_2$-N group, the $C_1\text{-}C_6$ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein $W^1$, $W^2$, and $W^3$ are each C-$R^4$, wherein $R^4$ is as defined above.

3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein one of $W^1$, $W^2$, and $W^3$ is N and the other two of $W^1$, $W^2$, and $W^3$ are each C-$R^4$, wherein $R^4$ is as defined above.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is $N(R^5)C(O)$ or C≡C.

5. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

6. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein n is 0.

7. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein n is 1.

8. The compound according to any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein $R^1$ is independently selected from:

5- or 6-membered heteroaryl-($C_1$-$C_8$ alkylenyl);
Substituted 5- or 6-membered heteroaryl-($C_1$-$C_8$ alkylenyl);
8- to 10-membered heterobiaryl-($C_1$-$C_8$ alkylenyl);
Substituted 8- to 10-membered heterobiaryl-($C_1$-$C_8$ alkylenyl);
Phenyl-($C_1$-$C_8$ alkylenyl); and
Substituted phenyl-($C_1$-$C_8$ alkylenyl); and

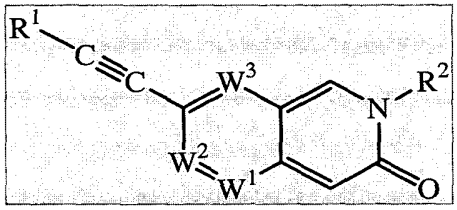
$R^2$ is independently selected from:

5- or 6-membered heteroaryl-($C_1$-$C_8$ alkylenyl);
Substituted 5- or 6-membered heteroaryl-($C_1$-$C_8$ alkylenyl);
8- to 10-membered heterobiaryl-($C_1$-$C_8$ alkylenyl);
Substituted 8- to 10-membered heterobiaryl-($C_1$-$C_8$ alkylenyl);
Phenyl-($C_1$-$C_8$ alkylenyl); and

Substituted phenyl-($C_1$-$C_8$ alkylenyl);

wherein each group and each substituent is independently selected.

9. The compound of Claim 1 of Formula II



II

or a pharmaceutically acceptable salt thereof.

10. The compound according to Claim 9, selected from:

4-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid tert-butyl ester;

4-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid;

2-(3,5-Difluoro-4-hydroxybenzyl)-7-[3-(4H-[1,2,3]triazol-4-yl)prop-1-ynyl]-2H-isoquinolin-3-one;

7-(3-Phenyl-prop-1-ynyl)-2-(4-trifluoromethylbenzyl)-2H-isoquinolin-3-one;

2-(3-Fluorobenzyl)-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-3-one;

4-[7-(3-Imidazol-1-ylprop-1-ynyl)-3-oxo-2H-isoquinolin-2-ylmethyl]benzoic acid tert-butyl ester;

4-[7-(3-Imidazol-1-ylprop-1-ynyl)-3-oxo-2H-isoquinolin-2-ylmethyl]benzoic acid;

3-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzonitrile;

4-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzenesulfonamide;

4-[3-Oxo-7-(3-[1,2,3]triazol-1-ylprop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid tert-butyl ester;

4-[3-Oxo-7-(3-[1,2,3]triazol-1-ylprop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid;

4-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid methyl ester;

3-[3-Oxo-7-(3-phenyl-prop-1-ynyl)-2H-isoquinolin-2-ylmethyl]benzoic acid methyl ester;

2-(4-Fluorobenzyl)-7-3-phenylprop-1-ynyl-2H-isoquinolin-3-one;

7-(3-Phenylprop-1-ynyl)-2-(3-trifluoromethylbenzyl)-2H-isoquinolin-3-one;

2-(3-Chlorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one;

2-(3,4-Difluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one; and

4-[1-Oxo-7-(3-[1,2,4]triazol-1-ylprop-1-ynyl)-2H-isoquinolin-3-ylmethyl]benzoic acid tert-butyl ester; or

a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

12. The pharmaceutical composition according to Claim 11, comprising a compound according to Claim 10, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

13. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

14. The method according to Claim 13, wherein the compound administered is a compound according to Claim 10, or a pharmaceutically acceptable salt thereof.